CONTROL OF FLUID BALANCE AND OSMOLARITY DISORDERS IN THE CEREBRAL PATHOLOGY

Eva Gheorghita, Cristina Bucur, Luminita Neagoe
ICU Department, "Bagdasar-Arseni" Emergency Clinical Hospital, Bucharest, Romania

ABSTRACT

Neurologically injured patients are at risk for osmolarity disorders. This is due to the fact that the brain controls the complex mechanism of the overall fluid balance and also possesses the capacity to locally minimize the plasma tonicity disturbances (cerebral osmoregulation).
Perioperative fluid administration, mannitol use, syndrome of inappropriate antidiuretic hormone and cerebral salt-wasting syndrome are potential causes of hyponatremia. Enteral tube feeding, osmotic diuresis and insipid diabetes are potential causes of hypernatremia.
Severe hyponatremia or severe hypernatremia have various neurological consequences. On the other hand, correction of these disorders must be done slowly, to avoid precipitating central pontine myelinolysis (for the case of correction of hyponatremia) or to avoid producing cerebral edema (for the case of correction of hypernatremia).

Key words: osmolarity, tonicity, hypersodemia, hyposodemia, mannitol, insipid diabetes, cerebral edema, water balance.

INTRODUCTION

The fluid balance is the outcome of a very complex machinery, under the control of the antidiuretic hormone (ADH), aldosteron and the natriuretic peptides.

The changes in the secretion of the ADH and of the natriuretic peptides, frequently met in the cerebral pathology, will directly influence the two fluidic compartments of the organism, the intracellular fluid (ICF) and the extra cellular fluid (ECF).

On the other side, changes in the sodium balance caused by a series of iatrogenic or pathological causes will have direct consequences, through the tonicity changes over the cerebral volume.

The brain, through the osmoregulation mechanism, possesses the capacity to minimize the plasma tonicity variations. Hence, the relationship between the cerebral pathology and the fluid equilibrium of the body is a bidirectional one, in which various cerebral affections have effects over plasma tonicity and volemia, but reversely as well, changes of intracellular hydration (edema or dehydration) make a mark on the state of consciousness and on the neurological status.

TERMS AND GENERAL CONCEPTS

1. Fluid compartments of the body

Total body water (TBW) is made 55-60% out of a man's body mass (BM) and 45%-50% of a woman's (the low percentage for the women is due to a higher proportion of the fat tissue than that for men). TBW is divided into two compartments:

– the extra cellular fluid (ECF) represents a third of TBW and approximately 20-25% of BM; it includes the plasma volume (PV) rich in sodium, proteins and interstitial fluid (ISF) poor in proteins;

ECF=PV+ISF

100%=25%+75%

Author for correspondence:
Eva Gheorghita, "Bagdasar-Arseni" Emergency Clinical Hospital, 12 Berceni Avenue, District 4, Zip Code 041915, Bucharest, Romania
email: gheorghita_eva@yahoo.com

– the intracellular fluid (ICF) represents two thirds from TBW and approximately 40% of BM; it is rich in potassium and poor in sodium.

Rule "20-40-60" ECF(20%)+ICF(40%)=TBW (60%) and

ECF(20%)=PV(5%)+ISF(15%)

(expressed percentages from BM)

2. Plasma osmolarity and plasma tonicity

Plasma osmolarity is defined by the concentration of osmoles contained by one liter of plasma (Osm/1).

Plasma osmolality is the concentration of osmoles in one kg of plasma (Osm/kg). In practice, the difference is negligible and the two terms are interchangeable.

The osmotic substances, according to the way they spread among the body's fluid compartments, are divided in:

- passive, diffusible substances: inactive osmoles represented by the urea (physiological present) and methanol, ethanol, etilenglicol (unknown to the body); they do not stimulate any osmotic transmembranary gradient, and therefore a water movement among the two compartments;
- active, requiring energy in order to spread/ diffuse: are represented by sodium, glucose usually found in ECF or unknown to the body (mannitol, glycerol); they determine an osmotic gradient and hence a water movement towards the more concentrated compartment from the more diluted compartment; they are responsible for the plasma tonicity.

The terms "isoosmotic", "hiperosmotic", "hipoosmotic" refer to the osmotic concentration of ECF in a state of equilibrium and are being used for describing changes in volume (dehydration, and over hydration).

The tonicity of a solution refers to the effect of that solution over the volume of a cell found in that solution:

- Isotonic – will not change the volume of the cell;
- Hypotonic – the cell will inflate causing cellular lyses;
- Hypertonic – the cell will shrink

Plasma osmolarity represents the sum of all plasmatic osmoles, active and inactive, dosed by ionogram Osmolarity =2x Na+, (mEq/l) + glycemia (mg/dl)/18 + urea (mg/dl)/2.8 normal values=280-295 mOsm/1.

The sodium concentration is doubled in order to include the concentration of chloride as well.

As it was reminded, plasma tonicity is given only by active osmoles, so that urea will disappear from the above formula for plasma osmolarity (275-290mOsm/1).

Analyzing the two concepts of tonicity and osmolarity, two conclusions are being emphasized:

a) there is a small difference of the value between tonicity and plasma osmolarity, so that the urea's contribution to the total concentration of osmoles from ECF is small;

b) sodemia is the main determinant for osmolarity and plasma tonicity and, implicitly, becomes the main determinant for the intracellular volume changes.

In practice, plasma tonicity determines intracellular hydration as follows: plasma hypertonicity is the cause for intracellular dehydration and reversely, plasma hypotonicity will determine intracellular hyperhydration, which, at a cerebral level, will translate through cerebral edema.

CONTROL OF THE WATER BALANCE

The hormonal control of the fluid balance is closely related to the proper functioning of the brain. The cerebral control over the proper release of ADH, the control of the hypothalamic-hypophysial tract over the cortex of the suprarenal gland that produces aldosteron, the release of the natriuretic peptides, the feeling of thirst that adjusts the water intake for the patient with a normal state of consciousness are the fundamental complex machinery that control the body fluid balance. It is easy to understand why cerebral pathology which modifies these mechanisms will have the most diverse and nocuous effects over the body's hydration state, over the structure of the various fluid compartments that will lead, by themselves, to the alteration of the state of consciousness and to the wide extension of the neurological consequences of the initial cerebral pathology, no matter its kind (vascular, malign, traumatic, and ischemic). Only the prompt and proper intervention of the hydroelectrolyte therapy, of suppression or hormonal administering, will succeed to "unchain" this vicious cycle and to reestablish the physiological machinery involved in the hydroelectrolyte homeostasis.

The main factors involved in the fluidic balance are hormonal (ADH and aldosteron), natriuretic peptides, the feeling of thirst.

1. The antidiuretic hormone (ADH) or vasopressin

This is a hypothalamic hormone synthesized in the paraventricular and supraoptic nuclei from the hypothalamus. Through the supraopticohypofisial tract it reaches the posterior lobe of the hypophysial gland from where it will be secreted. The main effect of ADH consists in adjusting the water excretion from the renal level: it connects to the specific receptors from the membrane of the distal tubes and renal collectors, increasing permeability and water reabsorption at this level and thus, decreasing the urinary water losses. Pathologically speaking, a less known effect of the ADH is found at the cerebral level, where by activating some specific receptors (aquaparine V2), the water penetration in the cells is being stimulated, leading to the increase of the cerebral edema. The effect is being noticed in the cerebral injury after the appearance of the focal ischemia. The main stimuli for the secretion of ADH are hyperosmolarity and the decrease in the circulatory blood volume (hypovolemia).

a) Hyperosmolarity represents the most important and sensitive stimuli for releasing the secretion of ADH; under normal circumstances, an increase of plasmatic osmolarity with 1-2% will determine the stimulation of the ADH secretion and reversely, with less than 280 mOsm/1, the secretion of the ADH becomes undetectable. The osmoreceptors are located in the anterior hypothalamus distinctly from the cells that synthesize the ADH. They are extremely sensitive to plasma osmolarity changes, as it was mentioned.

Only active osmoles (Na+, and mannitol) will stimulate the osmoreceptors and they are the potent stimulators for the ADH secretion. Since the plasma Na+, is responsible in a proportion of 95% for effective osmotic pressure, the osmoreceptors normally function as plasma receptors of Na+.

Hyperglycemia is a less potent stimulus of the ADH secretion, in contrast to hypernatremia, but in the uncontrolled diabetes, the high glycemia values will act as an effective stimulus for the ADH.

b) Hypovolemia. A decrease of 10-25% of the blood volume will produce the release of ADH. Hypovolemia is a less dominant stimuli for the secretion of ADH than hyperosmolarity (that is, nevertheless, a more sensitive stimuli). For example, under the circumstances of marked hyponatremia with hypovolemia, the inhibition of the secretion of ADH will not be produced, precisely with the purpose of maintaining the effective circulatory volume. The body fights more for maintaining the circulatory volume than for maintaining a normal osmolarity.

Baroreceptors and voloreceptors are situated in the atriums, the aortic arc, the carotid sinus, surrounding the large veins. Hypovolemia and the arterial hypotension will reduce the stimulating frequency of the baroreceptors, determining the stimulation of the secretion and the release of ADH.

Under cerebral pathologic circumstances (hypothalamus injury, seizures, stroke, meningitis, subdural hematoma) an excessive or improper ADH secretion might appear, known as syndrome of inappropriate secretion of ADH (SIADH). Also, in the cerebral pathology there are diseases that will suppress the secretion of ADH: adenomas and hypophysial tumors, craniopharingiomas, cerebral death.

2. Aldosteron is a corticoid hormone synthesized in the adrenalian cortex (the glomerulosa area).

The main effect of aldosteron consists in stimulating the retention of Na+ through the increase of Na+ reabsorption in the distal tubes and renal collectors. The reabsorption of Na+ is followed by water retention. At the same time, the secretion of K+ and H+ is being stimulated.

Through the increase of Na+ retention, the aldosteron adjusts the ECF volume. That is why the aldosteron adjusts the total of the Na+ content in the body, while the ADH adjusts the plasmatic concentration of Na+.

The stimuli for the secretion of aldosteron are the reninangiotensin system, hyperkaliemia, ACTH, and to a lower degree, hyponatremia.

a) The main stimulus for releasing aldosteron is the **reninangiotensin** system activated in his turn by a decrease in the effective circulatory volume (acute hypovolemia, acute hypotension).

b) Hyperkaliemia. An increase with 1% of kalemia stimulates the synthesis and the release of aldosteron through a direct action at the level of the glomerulosa area.

c) The hypothalamic-hypophisial-adrenocortical axis. The pituitary (hypophisial) gland is responsible for the secretion of the adrenocorticotropic (ACTH) hormone, also known as corticotrophin, which will stimulate the enzymes responsible for the synthesis of aldosteron. Corticotrophin

releasing hormone (CRH) is a hypothalamic polypeptide secreted in the portal hypophisial axis responsible for the release of ACTH from the pituitary gland.

Therefore, the central nervous system has a fundamental role in the sodium balance. The hypophisectomised patients, with pituitary insufficiencies show normal secretions of aldosteron at a moderate salt intake; yet, these people have showed a suboptimal response of aldosteron to the Na+ restriction.

d) Hyponatremia. A decrease of sodemia with 10% seems to stimulate the synthesis and release of aldosteron. Yet, this effect is canceled by the changes in the effective circulatory volume. Thus, the secretion of aldosteron is increased at the hyponatremic hypovolemic patients, but is decreased at the hyponatremic patients for whom the volemic repletion was undergone. Under clinical conditions, the appearance of edema in 90% of the hyponatremic patients is due to the stimulation of ADH and aldosteron caused by the decrease in the effective circulatory volume, the consequence being the increase of water retention, with the appearance of edema; so, over 90% of the clinical cases of hyponatremia are caused by a total excess of Na+ and a decrease in the circulatory blood volume and must be treated with the restriction of salt and water.

3. Natriuretic peptides are a group of polypeptides produced in various areas of the body

Three types are known: brain natriuretic (BNP), atrial (ANP) and C-type (CNP). The main effects are: renal loss of sodium and water (so, all the contrary effects produced by ADH), inhibition of the secretion of aldosteron and rennin, decrease in the arterial systemic pressure and bradicardia. These hormones do not only have systemic effects, but it has been proven that, in cerebral pathology that causes cerebral edema, the content of water and sodium will be reduced in the areas of cerebral edema through the direct influence of permeability of the cerebral capillaries. Also, ANP raises the cerebral blood flow and determines significant cerebral vasodilatation.

The pathological release of these hormones (even the ANP is produced in the cerebral areas: hypothalamus, choroids plexus, median eminence, spine) in various cerebral affections it produces the "cerebral salt-wasting" syndrome.

4. The feeling of thirst represents a primordial control mechanism of the water balance through the adjustment of the exogen water intake

Thirst appears under conditions of hypovolemia or arterial hypotension. For a plasmatic osmolarity over 290-295 mOsm/1, simultaneously with the increase of ADH, thirst is being stimulated; it has no superior limit and will correct the plasmatic hypertonicity. Theoretically, the plasma hipertonicity can be developed only in the absence of thirst or in the impossibility to drink.

For the patients who have the hypothalamic center of thirst affected or for the comatose patients or with psychiatric or neurological diseases, the water balance will not benefit of correction through water ingestion, dehydration and hypernatremia being produced.

Next, we will discuss the practical aspects related to the osmolarity disorders in cerebral pathology, as well as the neurological consequences induced by sodemia changes, as the most important determinant of plasma tonicity.

HYPONATREMIA AND CEREBRAL OSMOREGULATION

When applied, the most majority of the hyponatremias are almost always associated with hypotony, which will cause intracellular hyperhydration.

At a cerebral level, hyponatremia will determine the cerebral edema and intracranial hypertension, the more nocuous as the increase of the cerebral volume is acute. Yet, the brain possesses the means to minimize the variations of the volume induced by the plasma hypo- or hypertonia. This process is called "cerebral osmoregulation" and is due to a modulation of the intracerebral content of the active osmoles (osmoprotective molecules) that are of two kinds:

- inorganic: electrolytes (Na+, K+, C1-);
- organic: amino acids, polios, trietilamine.

Under conditions of intracerebral hyperhydration, the brain tries to protect itself from the increase of the cerebral volume through the removal of osmoprotective electrolytes (the acute phase). This mechanism appears in the first 30 minutes from the appearance of the cerebral edema, but is unfinished, for it will lead to the attenuation of the cerebral edema and not to its disappearance. In the slowly established plasma hypotonia (chronic hyponatremia), osmoregulation is mainly done by decreasing the intracerebral content of organic idiogen osmoles. This mechanism works much slowly

but is more complete as in the case of acute situations, so that the cerebral edema is cvasinexistent in the chronic hyponatremias.

Under circumstances of a cerebral tumor, induced cerebral hypoxia or hypoperfusion, the efficiency of cerebral osmoregulation is impaired, so that in cerebral pathology, this protective mechanism is almost canceled. Also, to the female who is genitally active, the estrogens and progesterone inhibit the functioning of the Na+, K+, ADP-dependent pumps, which leads to the limitation of the adjustment of the cerebral volume through this mechanism.

There are rare situations of hyponatremia associated with normal plasma tonicity (for ex. hyperlipidemias or hyperproteinemias) or with increased plasma tonicity (for ex. hyperglicemia, treatments with mannitol) known as false hyponatremias.

In the medical practice from the cerebral pathology, the following hyponatremias must be reminded.

1. The initial hyponatremia from the treatment with mannitol

The mannitol used in the cerebral edema therapy, is an active osmole that will lead to hyperosmolarity and a plasma hypertony responsible for the water transfer from ICF to ECF. Initially, a dilution hyponatremia will be induced, accompanied by intracellular dehydration (and, so, intracerebral). Subsequently though, due to the appearance of osmotic dieresis as well, if the treatment with mannitol is not associated to the correction of the urinary water losses through exogen liquid intake, it can lead to the contraction of extra cellular space and to hipernatremia. That is why maintaining euvolemia is absolutely necessary.

There are other aspects less known in the extended practice of therapy with mannitol for correcting cerebral edema. The whole brain is not permeable to water and osmoles due to the specifics of blood brain barrier (BBB), as are the systemic capillaries or the affected BBB by various causes. That is why the mannitol has a low osmotic effect over the normal brain, lowering the water content from the cerebral level with only 2-6%. This osmotic effect appears after 15-30 minutes from administering and persist up to 1.5-7 hrs. It is more emphasized after the first doses and becomes less effective at the following doses (dose 3,4). If it is administered in higher or multiple doses, the mannitol will go across an affected BBB and will interstitially cumulate, exacerbating the cerebral edema, contrary to the wanted therapeutic effect.

From the less known benefic therapeutic effects of the mannitol at a cerebral level, the following must be reminded: the vasoconstrictive action over cerebral microvascularization, decreasing viscosity, increasing the cerebral blood flow and the scavenger activity over the free radicals.

Next, we will discuss the main situations of hypotonic hyponatremias met in the cerebral pathology.

2. The syndrome of inappropriate secretion of ADH (SIADH)

SIADH is characterized by an excessive or improper secretion of ADH, which will determine a high natriuresis in proportion to the plasma hypotonia (abnormal antidiuresis with water retention). While the syndrome becomes chronic, the natriuresis can decrease simultaneously to the loss of the body's sodium capital.

Therefore, the patients will show sings of:

- hyponatremia (Na+<134m Eq/1) and low plasmatic osmolarity (<280m Osm/1);
- normal or high ECF; in a first phase, edema can appear because of hypoosmolarity that will lead to the water shift in the interstitial space; these appear in case the water ingestion is done normally; if the water ingestion is restricted, the water retention and edema do not appear anymore (ECF is normal);
- high or normal urinary Na+ (urinary Na+>18mEq/l).

The main causes for SIADH are as follows:

- CNS pathology: seizures, infections, brain injury, cerebral tumors, sinus cavernous thrombosis, cerebral atrophy, hydrocephaly, stroke, post anoxic encephalopathy, periphery neuropathy, multiple sclerosis, delirium tremens;
- pleuropulmonary pathology: pulmonary cancers, infections, ARDS, ventilation with positive pressure, asthma, pneumotorax;
- various neoplasias;
- treatments with: oxitocine, desmopresine, carbamazepin, cytostatics, IMAO, neuroleptics;
- postoperative period.

The differential diagnostic is done with the hyponatremias associated to the mineral corticoid insufficiencies and hypothyroidism which, through aldosteron dysfunction, encourages sodium depletion and stimulation of ADH.

The treatment of SIADH consists in the slow increase of the sodium capital and restriction of the

liquid intake at 800-1500ml/day (under the daily dieresis volume). In severe cases of SIADH, furosemide is being administered (it produces a watery diuresis) and, also, NaCI 3% solution. As a specific treatment, 150-300mg/6h of phenytoin or demeclociline can be administered in order to inhibit the ADH.

3. Potomania (psychotic polidipsia) or the water intoxication syndrome

Is an affection that leads to hyponatremia and is met in the medical practice of the psychiatric pathology (schizophrenia, acute psychosis). It is also a part of the group of hypotonic hyponatremias with normal ECF.

4. Cerebral salt-wasting syndrome (CSW)

CSW leads to a hypotonic hypovolemic hyponatremia and it is caused by the release of natriuretic peptides from the hypothalamus, in the attempt to increase the cerebral blood flow. It is usually met in subarahnoidian hemorrhage (SAH) of any type (traumatic or vascular) and the release of the natriuretic factors may improve, through induced cerebral vasodilatation, the vasospasm. CSW usually appears after 3-7 days from the appearance of SAH, simultaneously with the appearance of the vasospasm.

The CSW diagnostic includes:

- hyponatremia (Na+<134mEq/1) with a hypoosmolarity (<280mOsm/1);
- high urinary Na+ (urinary Na+ >18mEq/1);
- low ECF (differential diagnostic with SIADH), therefore hypovolemia.

The treatment will follow the recovery of the volemic deficit and of the sodium capital by administering hypertonic solutions 3% of NaC1, at a rate of 10-50ml.

The neurological symptoms of hyponatremia appear at values of Na+<120mEq/1 and include: headache, confusion, lethargy, vomiting, muscular cramps and depressed deep tendon reflexes, seizures. Not treating an acute hyponatremia might severely involve to coma and death.

The treatment of hyponatremia targets the recovery of the sodium capital and is different in function of the gravity and way of establishment of the hyponatremia. The necessary quantity of NaC1 to increase sodemia (Na+ deficit) is estimated according to the formula:

Na+deficit(mEq) = 0.6 x BM(kg) x (desired Na+ – current Na+)

Knowing that 0.9% Na Cl (isotonic normal saline) solution contains 154mEq/1of Na+, conforming to this formula, the volume of the necessary normal saline can be appreciated for treating hyponatremia. In order to decrease the iatrogenic liquid volume for treatment the hyponatremias that do not accompany the decrease of ECF (e.g. SIADH), solutions that have a greater concentration of mEq NaC1 can be used (3% hypertonic NaCl solution).

A correction of hyponatremia that is too fast was associated with demyelization lesions in the pons, which lead to permanent neurological damage. In this situation, fluctuations of the state of consciousness appear, as well as convulsions, akinetic mutism, hypoventilation and hypotension. In severe forms, pseudo bulbar palsy may appear: dysphasia, disartrie, tetra paresis, "locked-in" syndrome. The patients evolve to coma and death. The diagnostic can be given with the help of MRI, but is generally confirmed by the anatomopathologic result of the autopsy.

The risk factors for central demyelization lesions are: a correction of sodium that is too fast, as well as the alcoholic patients, malnourished patients, burned people, hypokalemia, hypoxia.

The rapidity by which the correction of hyponatremia must be done is related to the gravity of the symptoms. The following rates of correction are being indicated: for minimal symptoms, 1 mEq/1/h or less; for moderate symptoms 1.5 mEq/l/h; for severe symptoms 2-2.5 mEq/1/h.

Correcting acute hyponatremia is made with hypertonic serum NaCl 3% and with a loop diuretic (furosemide). If the neurological signs have disappeared or the natremia has reached 130 mEq/1/h, the administering of hypertonic serum 3% must be stopped and it will continue with physiological 0.9% serum.

Correction of chronic symptomatic hyponatremia is done with hypertonic serum for the correction of sodium with 1.5 mEq/1/h, as well as with furosemide and after Na + reaches 130 mEq/l, with water restriction (<800 ml/day). The antagonists V2 of the ADH receptors (known as aquaretics) represent a modern treatment of asymptomatic chronic hyponatremia (chronic SIADH).

THE CHARACTERISTICS OF HYPERNATREMIA IN CEREBRAL PATHOLOGY

Hypernatremia is always a cause for hyperosmolarity and is almost always the result of the loss of water in excess of sodium (loss of hypotonic fluids) or the retention of a large sodium quantity.

Even when the urine concentration capacity of the kidney is affected, the thirst is always the mechanism that prevents the appearance of hypernatremia. That is why, hypernatremia is frequently met at the senile patients or comatose patients, that is exactly in the cerebral pathology, these being the category that can not adjust the water ingestion. Two other hypernatremic situations in the neurosurgical practice must be reminded: hypernatremia from the iatrogenic polyuria and that from the insipid diabetes.

1. Polyuria from the treatment with mannitol

As it was recalled, if the treatment with mannitol applied for the improvement of the cerebral edema is not associated to the correction of the volemic deficit caused by the induced osmotic polyuria, hypernatremia appears instead of hyponatremia. This becomes the marker for extra cellular and intracellular iatrogenic dehydration, with the most severe consequences over the brain, that we will remind in the following.

2. Central insipid diabetes

Hypothalamic or hypophysial gland injuries (basilar skull fractures), craniopharingiomas, pituitary gland surgery, frequently produce insipid diabetes. A transitory insipid diabetes is frequently associated to the postoperative period after the neurosurgical procedures and to the brain injuries. Another cause for central insipid diabetes which causes brutal hypernatremia is cerebral death.

The diagnostic is suggested by polydipsia, polyuria (often>61/day), with low urinary osmolarity.

The parameters will include:

- increased urinary debit (>250ml/h);
- massive water losses through urine compared to the losses of sodium, which will lead to increased values of sodemia (at the superior limit or over the normal values);
- low urinary osmolarity in proportion to plasma (50-150 mOsm/1);
- low urinary Na+ (30-50 mEq/1);
- plasma hyperosmolarity (>290-295 mOsm/1).

It is to be mentioned the fact that, due to the stimulation of thirst, polydipsia appears, so that the majority of the patients with insipid diabetes maintain their water balance and have a normal or cvasinormal sodemia (isovolemic hypernatremia).

In the cerebral pathology, however, the patient can not compensate by water intake the urinary water loses, so therefore hypernatremia quickly develops as a witness for extra- and intracellular dehydration.

3. Enteral tube feeding, needed for nourishing the comatose patients

It may predispose to a low ECF hypernatremia due to the osmotic diarrhea that may appear. Some enteral tube feedings have a high content of lipids, proteins and sugars, being high osmolar and causing osmotic diarrhea.

The clinical symptoms of hypernatremia are the ones of severe dehydration and values of Na+ >150 mEq/1 appear: thirst, dryness of the mucosa, the decrease of arterial pressure correlated to the increase of the ventricular rate, turgor of the skin, hypercrom urine (excepting the polyuria from the insipid diabetes), weight loss. The neurological signs frequently dominate the clinical picture: altering the state of consciousness going from irritability till stupor and coma, the appearance of mioclonias, hyperreflexia and seizures. The anatomic lesions responsible for these neurological signs can be of hemorrhagic kind (intraparenchimatous petechiae, intracerebral hemorrhage and subdural hematomas) or of thrombotic kind (thrombosis of the small cerebral veins and of the cerebral sinuses), as a consequence of hypercoagulability associated with hypernatremia.

The symptoms more closely correlate with the speed of water movement in the brain and less with the absolute value of hypernatremia. Chronic hypernatremia is much more tolerated than the acute one. Fever, tachypnea, asthenia can appear.

The cerebral osmoregulation mechanism also intervenes in the case of hypernatremia by the increase of the inositol and of the aminoacids (glutamine and taurine) in the intracellular space, which leads to the slow recovery of the neuronal content of water.

TREATMENT

Hipernatremia with hypovolemia and hypotension must be avoided and immediately corrected, for in a single episode of hypotension it doubles the morbidity and death rate from the severe head injury.

The amount of fluid deficit needed to correct the hypernatremia will be calculated according to the formula:

Fluid deficit (1) = 0.6 x BM (kg) x (1- 140/ current Na+)

This amount of fluid must be corrected over the course of 48h. It is used a hypotonic solution (NaC1

0.45% or glucose 5%) in the first days and a lesser hypotonic solution (lactated Ringer) thereafter. A faster correction of hypernatremia may cause seizures, cerebral edema, permanent neurological damage and even death. Sodemia must be monitorized by serried blood samples. Generally, sodemia must not be lowered than 0.5-1 mEq/1/h, especially for old age persons.

In the case of central insipid diabetes, the etiological treatment is associated. Exogen vasopresin (5units sc./4hr) is administered. Desmopresin (dDVAP) is a synthetic analog of ADH with an action period of 12-24hr and is available in intranasal administering (5-10mg/dose).

CONCLUSION

In conclusion, the osmolarity disorders frequently met in the intensive therapy are most of the time caused by changes in sodemia. The clinical manifestations have a direct neurological target, for they will alter the content of water at the cerebral level with the most severe consequences over morbidity and death rate.

For the comatose patient who can not correct his/her water intake, the fluid balance must be maintained by the treatment of the neurologist, the neurosurgeon or intensive therapy doctor.

The picture becomes more complex, because one must consider the existence of the syndromes from the cerebral pathology that produce themselves changes of osmolarity.

The therapy for these disorders of osmolarity is specific for the various illnesses producing them, but it is also oriented to general therapy towards maintaining the fluid balance, on one side, and towards the correction of the sodium capital on the other side.

REFERENCES

1. Siddiqi J – Neurosurgical intensive care. New York: Thieme Medical Publishers 2008; 21:290- 310
2. Morgan GE – Clinical Anesthesiology 2-nd ed. Stamford, Connecticut: Appleton & Lange 1996; 29:543-558
3. Bullock J – Physiology 3-rd ed. Malvern, PA.: Williams & Wilkins, 1995
4. Ichai C et al – Hyponatremies en reanimation. Anesthesie- Reanimation vol.5; 2002; Paris: Editions Scientifiques et Medicales Elsevier SAS 36-860-A-05
5. Baghdadi H et al – Conduite a tenir devant une hypernatremie. Anesthesie- Reanimation vol.5; 2002; Paris: Editions Scientifiques et Medicales Elsevier SAS 36-860-A-10
6. Andrews BT – Fluid and electrolyte disorder in the neurosurgical intensive care. *Neurosurg Clin N AM* 1994; 5:707-723
7. Ropper A – Fluid and metabolic derangements. Neurological and Neurosurgical Intensive Care. 4-th ed. Philadelphia: Lippincot Williams & Witkins 2004; 105-112
8. Kaufmann AM – Aggravation of vasogenic cerebral edema by multiple-dose mannitol. *J Neurosurg* 1992; 77:584-589
9. Yao FS – Problem-oriented patient management. 6-th.ed. Philadelphia: Lippincot Williams & Withkins; 2008; 22:527-548; 597-616
10. Vialet R et al – Isovolume hypertonic solutes (sodium chloride or mannitol) in the treatment of refractory posttraumatic intracranial hypertension: 2 ml/kg 7,5% saline is more effective that 2 ml/kg 20 mannitol. *Crit Care Med* 2003; 31:1683-1687
11. Cucchiara RF et al – Clinical neuroanesthesia, 2-nd ed. New York: *Churchill Livingstone,* 1998:241-242